

THAT WHICH IS CLAIMED:

1. An isolated nucleic acid comprising a degenerate variant of the nucleotide sequence of SEQ ID NO:1 having a GC content from about 55% to about 67%.
- 5 2. The nucleic acid of Claim 1, wherein GC content is effective for enhancing heterologous expression of said nucleic acid in enteric bacteria.
3. The nucleic acid of Claim 1, further comprising a plurality of codons having a substitute base at a wobble position, said plurality of codons selected from the group of codons encoding alanine, arginine, glutamate, glycine, and 10 valine.
4. The nucleic acid of Claim 1, wherein wobble position GC content is effective for enhancing efficiency of a polymerase-based methodology with said nucleic acid.
5. The nucleic acid of Claim 4, wherein said polymerase-based 15 methodology is selected from PCR, mutagenesis, and sequencing.
6. The nucleic acid of Claim 1, further comprising an expression vector operably linked to an expression control sequence.
7. The nucleic acid of Claim 1, wherein an isolated cell comprises said nucleic acid and an expression vector therefor operably linked to an expression control sequence.
8. The nucleic acid of Claim 1, wherein an isolated cell comprises said nucleic acid operably linked to an expression control sequence.

9. The nucleic acid of Claim 1, further comprising an expression vector wherein said nucleic acid is operably linked to an expression control sequence, and wherein an isolated cell or a progeny of said cell is transfected with said vector.
- 5 10. An isolated nucleic acid comprising a sequence having a GC content of from about 55% to about 67% and encoding a polypeptide having the amino acid sequence of SEQ ID NO:5.
11. The nucleic acid of Claim 10, further comprising a plurality of codons having a substitute base at a wobble position, said plurality of codons selected
10 from the group of codons encoding alanine, arginine, glutamate, glycine, and valine.
12. The nucleic acid of Claim 10, wherein wobble position GC content is effective for enhancing efficiency of a polymerase-based methodology with said nucleic acid.
- 15 13. The nucleic acid of Claim 12, wherein said polymerase-based methodology is selected from PCR, mutagenesis, and sequencing.
14. The nucleic acid of Claim 10, further comprising an expression vector operably linked to an expression control sequence.
15. The nucleic acid of Claim 10, wherein an isolated cell comprises said
20 nucleic acid and an expression vector therefor operably linked to an expression control sequence
16. The nucleic acid of Claim 10, wherein an isolated cell comprises said nucleic acid operably linked to an expression control sequence.

17. The nucleic acid of Claim 10, further comprising an expression vector wherein said nucleic acid is operably linked to an expression control sequence, and wherein an isolated cell or a progeny of said cell is transfected with said vector.
- 5 18. The nucleic acid of Claim 10, wherein said GC content is effective for producing an average codon bias in enteric bacteria of from greater than about 44% up to about 66% so as to thereby enhance heterologous expression thereof.
- 10 19. An isolated nucleic acid comprising a degenerate variant of the nucleotide sequence of SEQ ID NO:3 having a GC content from about 56% to about 70%.
20. The nucleic acid of Claim 19, wherein GC content is effective for enhancing heterologous expression of said nucleic acid in enteric bacteria.
- 15 21. The nucleic acid of Claim 19, further comprising a plurality of codons having a substitute base at a wobble position, said plurality of codons selected from the group of codons encoding alanine, arginine, glutamate, glycine, and valine, said substitute base effective for reducing GC content of said nucleic acid.
- 20 22. The nucleic acid of Claim 19, wherein wobble position GC content is effective for enhancing efficiency of a polymerase-based methodology with said nucleic acid.
23. The nucleic acid of Claim 22, wherein said polymerase-based methodology is selected from PCR, mutagenesis, and sequencing.

24. The nucleic acid of Claim 19, further comprising an expression vector operably linked to an expression control sequence.
25. The nucleic acid of Claim 19, wherein an isolated cell comprises said nucleic acid and an expression vector therefor operably linked to an
5 expression control sequence.
26. The nucleic acid of Claim 19, wherein an isolated cell comprises said nucleic acid operably linked to an expression control sequence.
27. The nucleic acid of Claim 19, further comprising an expression vector wherein said nucleic acid is operably linked to an expression control
10 sequence, and wherein an isolated cell or a progeny of said cell is transfected with said vector.
28. An isolated nucleic acid comprising a sequence having a GC content of from about 56% to about 70% and encoding a polypeptide having the amino acid sequence of SEQ ID NO:6.
- 15 29. The nucleic acid of Claim 28, further comprising a plurality of codons having a substitute base at a wobble position, wherein said substitute base is effective for enhancing heterologous expression in *Escherichia coli* of a polypeptide encoded by said nucleic acid.
- 20 30. The nucleic acid of Claim 29, wherein said plurality of codons is selected from the group of codons encoding alanine, arginine, glutamate, glycine and valine

31. The nucleic acid of Claim 28, wherein wobble position GC content is effective for enhancing efficiency of a polymerase-based methodology with said nucleic acid.

32. The nucleic acid of Claim 31, wherein said polymerase-based
5 methodology is selected from PCR, mutagenesis, and sequencing.

33. The nucleic acid of Claim 28, further comprising an expression vector operably linked to an expression control sequence.

34. The nucleic acid of Claim 28, wherein an isolated cell comprises said nucleic acid and an expression vector therefor operably linked to an
10 expression control sequence.

35. The nucleic acid of Claim 28, wherein an isolated cell comprises said nucleic acid operably linked to an expression control sequence.

36. The nucleic acid of Claim 28, further comprising an expression vector wherein said nucleic acid is operably linked to an expression control
15 sequence, and wherein an isolated cell or a progeny of said cell is transfected with said vector.

37. The nucleic acid of Claim 28, wherein said GC content is effective for producing an average codon bias in enteric bacteria of from greater than about 41% to about 68% so as to thereby enhance heterologous expression
20 thereof.

38. A method of making a nucleic acid sequence encoding a polypeptide according to SEQ ID NO:5 and having enhanced efficiency in a polymerase-based methodology, the method comprising synthesizing a degenerate variant

of a nucleic acid sequence according to SEQ ID NO:1 wherein a plurality of codons comprises at least one base substitution effective for sufficiently reducing GC content of said degenerate variant nucleic acid sequence to thereby enhance efficiency of the polymerase-based methodology.

5 39. The method of Claim 38, wherein the polymerase-based methodology is selected from PCR, mutagenesis, and sequencing.

40. A method of making a polypeptide, comprising culturing an isolated cell transfected with a synthetic nucleic acid comprising a degenerate variant of the nucleotide sequence of SEQ ID NO:1 having a GC content of from about 10 55% to about 67%, and an expression vector therefor operably linked to an expression control sequence, wherein culturing is effected under conditions permitting expression of said nucleic acid so as to produce a polypeptide encoded thereby.

15 41. The method of Claim 40, further comprising purifying the polypeptide from the cell or from the medium.

42. A method of making a polypeptide, the method comprising culturing an isolated cell transfected with a synthetic nucleic acid comprising a sequence having a GC content of from about 55% to about 67% encoding a polypeptide having the amino acid sequence of SEQ ID NO:5, and an expression vector 20 therefor operably linked to an expression control sequence, wherein culturing comprises conditions permitting expression to produce the polypeptide.

43 The method of Claim 42, further comprising purifying the polypeptide from the cell or from the medium.

44. A method of making a polypeptide according to SEQ ID NO:5 having enhanced expression in an enteric bacterium, the method comprising:

synthesizing a degenerate variant of a nucleic acid sequence encoding the polypeptide, wherein a plurality of codons comprises a base substitution at a wobble position effective for reducing GC content in the nucleic acid sequence; and

expressing the nucleic acid sequence in the enteric bacterium under conditions effective for production of the polypeptide encoded thereby.

10 45. The method of Claim 44, wherein the enteric bacterium comprises *Escherichia coli*.

46. A method of making vitamin C, comprising the reduction of 2,5-diketo-D-gluconic acid to 2-keto-L-gulonic acid by a polypeptide according to SEQ ID NO:5 expressed from a nucleic acid comprising a degenerate variant of the 15 nucleotide sequence of SEQ ID NO:1 having a GC content of from about 55% to about 67%.

47. A method of making a nucleic acid sequence encoding a polypeptide according to SEQ ID NO:6 and having enhanced efficiency in a polymerase-based methodology, the method comprising synthesizing a degenerate variant 20 of a nucleic acid sequence according to SEQ ID NO:3 wherein a plurality of codons comprises at least one base substitution effective for sufficiently reducing GC content of said degenerate variant nucleic acid sequence to thereby enhance efficiency of the polymerase-based methodology

25 48. The method of Claim 47, wherein the polymerase-based methodology is selected from PCR, mutagenesis, and sequencing.

49. A method of making a polypeptide, comprising culturing an isolated cell transfected with a synthetic nucleic acid comprising a degenerate variant of the nucleotide sequence of SEQ ID NO:3 having a GC content of from about 56% to about 70%, and an expression vector therefor operably linked to an expression control sequence, wherein culturing is effected under conditions permitting expression of said nucleic acid so as to produce a polypeptide encoded thereby.

5 50. The method of Claim 49, further comprising purifying the polypeptide from the cell or from the medium.

10 51. A method of making a polypeptide, the method comprising culturing an isolated cell transfected with a synthetic nucleic acid comprising a sequence having a GC content of from about 56% to about 70% encoding a polypeptide having the amino acid sequence of SEQ ID NO:6, and an expression vector therefor operably linked to an expression control sequence, wherein culturing comprises conditions permitting expression to produce the polypeptide.

15 52. The method of Claim 51, further comprising purifying the polypeptide from the cell or from the medium.

20 53. A method of making a polypeptide according to SEQ ID NO:6 having enhanced expression in an enteric bacterium, the method comprising:
synthesizing a degenerate variant of a nucleic acid sequence encoding the polypeptide, wherein a plurality of codons comprises a base substitution ~~non~~ at a wobble position effective for reducing GC content in the nucleic acid sequence; and

25 expressing the nucleic acid sequence in the enteric bacterium under conditions effective for production of the polypeptide encoded thereby.

54. The method of Claim 53, wherein the enteric bacterium comprises *Escherichia coli*.
55. A method of making vitamin C, comprising the reduction of 2,5-diketo-D-gluconic acid to 2-keto-L-gulonic acid by a polypeptide expressed from a nucleic acid comprising a degenerate variant of the nucleotide sequence of SEQ ID NO:3 having a GC content of from about 56% to about 70%.
56. A method of making a nucleic acid sequence encoding a polypeptide having a wild type amino acid sequence according to SEQ ID NO:1 or SEQ ID NO:3 and enhanced heterologous expression in enteric bacteria, the method comprising synthesizing a degenerate variant of the nucleic acid sequence wherein a plurality of codons comprises a base substitution effective for reducing GC content.
57. The method of Claim 56, wherein the GC reduction is made in a plurality of codon wobble positions.
- 15 58. The method of Claim 56, wherein *Escherichia coli* is the enteric bacteria.